An application of a mathematical blood flow model

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Abstract

Mathematical models of blood flow are inevitably embedded in models of human thermoregulation because they take the role of the most significant heat distributor in models of the human thermal system [14, 6]. Models of human thermoregulation have a wide range of applications, e.g. for the prediction of the impact of accidents, diseases and clinical treatments (see [14] and the references therein). The application of our interest is the prediction of the influence of cooling on the heat distribution in premature infants, see Section 2. In Section 3 we discuss the requirements of a reliable thermoregulation model while the governing equation is described in paragraph four. The employed blood flow model is discussed within Section 5. Section 6 deals with numerical results, followed by concluding remarks in the last paragraph.

1 Motivation

Lack of oxygen of the fetus or newborn is known to be an important cause for injuries of the developing brain [9]. Experimental studies have shown that the neuronal loss evolves over several days after such an incident [8]. An important factor influencing the degree and distribution of neuronal loss is the cerebral temperature, i.e. lowering the cerebral temperature can prevent much damage [5].

The question arises, if it is possible to lower the cerebral temperature of an infant by $2-3\,K$ by the manipulation of the environment inside an incubator while the rest of the body maintains a pleasant temperature. The objective of this paper is to discuss the mathematical measurements which can be used to predict an answer to that question by the use of numerical simulations.

2 Modeling the thermoregulation of premature infants

The term thermoregulation stands for the measurements of the body to hold a pleasant temperature [4]. Models for thermoregulation consist of two parts: the active and the passive system [6]. The active system consists of the regulatory mechanisms shivering (heat production within the muscles attached to the skeleton), vasomotion (control over the degree of blood flow within the skin) and sweating (control over the degree of effectiveness of heat transfer between the infant and the surrounding air). The passive system

is the combination of the physical human body and the heat transfer in it and at its surface. The idea behind this distinction is that the active system has a controlling influence over the passive system. Naturally, only results obtained by the complete model can be compared with available real life data.

Concerning premature infants, it is known that shivering and sweating are not of importance for the modelling process [4, 13], while vasomotion should not be of great concern for our special application [13]. The modeling of the passive system demands the discretization of the body and the modeling of metabolic heat production and blood flow. We do not consider phenomena which are related to environmental conditions, namely the response to air convection, the probability to gain or loose heat due to radiation and heat loss due to evaporation in dependence on pressure, temperature and humidity of the surrounding air, assuming that these are controllable by the use of an incubator [13].

In order to give an answer to the defined question by use of numerical simulations, a model needs to deliver detailed temperature profiles within the head and a detailed resolution of the heat transfer processes in the body. It should be applicable to different size neonates whereby aspects like the anatomy and the thermal maturity have to be considered. With the exception of the blood flow model, these aspects can be defined via a suitable geometry and the use of real life data for spatially dependent rates of metabolic heat production within a numerical method [7, 2]. This also incorporates that existing numerical methods made for the simulation of thermoregulation of adults are of no use in the given context since studies have shown [3] that a detailed modeling of geometry and tissue composition is necessary in order to obtain relevant temperature profiles. As it can be shown experimentally [7, 2] in agreement to theoretical discussions concerning thermoregulation models of adults [6, 14], the use of a blood flow model greatly affects the computed numerical solutions.

3 Analysis of the blood flow model

The bio-heat equation derived by Pennes [10] forms the basis of the majority of models for human thermoregulation in use today [14, 6]. It describes the dissipation of heat in a homogeneous, infinite tissue volume. For two spatial dimensions, it can be written in the form

$$c(\mathbf{x})\rho(\mathbf{x})\partial_t T(\mathbf{x},t) = \operatorname{div}\big[\lambda(\mathbf{x})\nabla \mathrm{T}(\mathbf{x},\mathrm{t})\big] + \mathrm{f}(\mathbf{x},\mathrm{t}). \tag{3.1}$$

Thereby, the temperature T depends on the spatial variable $\mathbf{x} = (x_1, x_2)^T$ as well as on time t. Furthermore, $\lambda(\mathbf{x})$, $c(\mathbf{x})$ and $\rho(\mathbf{x})$ denote the heat conductivity, specific heat capacity and density of the tissue, respectively. The term $f(\mathbf{x})$ can be decomposed via $f(\mathbf{x},t) = Q_M(\mathbf{x}) + Q_B(\mathbf{x},t)$ into parts corresponding to metabolic heat production $Q_M(\mathbf{x})$ and blood flow $Q_B(\mathbf{x},t)$.

As already indicated, the term $Q_M(\mathbf{x})$ can be defined by the use of real life data [7]. The formulation of the source term due to blood flow is based on variations of the following procedure [6, 14]. The idea is that the body is supplied from a central pool of blood by the major arteries. Before the tissue is perfused, the temperature of the arterial blood mixes with the temperature of venous blood flowing in adjacent veins. After that, the arterial blood exchanges heat with the tissue in the capillaries and becomes venous

blood. The venous blood is collected in the major veins and its temperature mixes with the temperature of arterial blood in the adjacent arteries before it flows back into the blood pool.

Since equation (3.1) deals with the change of thermal energy per unit volume, the term $Q_B(\mathbf{x})$ takes the form

$$Q_B(\mathbf{x},t) = c_B \rho_B CCX(\mathbf{x}) BF(\mathbf{x}) \big[T_B(t) - T(\mathbf{x},t)\big], \tag{3.2}$$

whereby $T_B(t)$ denotes the time-dependent mean value of the temperature of the blood within the blood pool, we also assume that the specific density of the blood ρ_B and the specific heat capacity of the blood c_B are constant variables.

The described modeling results in a differential equation for the temporal evolution of the temperature within the blood pool, namely in

$$m_B c_B \partial_t T_B(t) = \int_D \rho_B c_B CCX(\mathbf{x}) BF(\mathbf{x})\, d\mathbf{x} \big[T_V(t) - T_B(t)\big]. \tag{3.3}$$

Thereby, the total blood mass m_B, the time dependent mean value of the temperature of the venous blood $T_V(t)$, and locally defined tissue-dependent measures for the blood perfusion $BF(\mathbf{x})$ and the counter-current heat exchange $CCX(\mathbf{x})$ are introduced.

Equation (3.3) shows that the temporal change of the blood pool temperature is proportional to the difference to the temperature of the venous blood. The outlined idea leads to the modeling of the temperature of the venous blood as

$$T_V(t) = \frac{\int_D CCX(\mathbf{x}) BF(\mathbf{x}) T(\mathbf{x},t)\, d\mathbf{x}}{\int_D CCX(\mathbf{x}) BF(\mathbf{x})\, d\mathbf{x}} \tag{3.4}$$

which is also usable when only steady states are considered [7]. The crucial terms in the order of importance are the blood perfusion $BF(\mathbf{x})$ and the counter current heat exchange $CCX(\mathbf{x})$.

There is much debate about the choice of these functions in literature [14, 6]. This debate arises because the representation of blood circulation is substituted by a rather simple model formulation. The cure to this disadvantage is generally sought by exploring more and more detailed models of microstructure, organs, etc., or it is sought by a better modeling of control mechanisms of the actice system in the case of adults [14, 6].

The main drawback of the described blood flow model is given by the blood pool idea itself. This is up to now to our knowledge not outlined in any mathematical description of this model within the literature and can be illustrated as follows. Let a detailed geometry be given with a stationary temperature distribution together with a homogeneous neutral temperature at the whole boundary as initial state. Let us assume that we start a numerical computation where a selective cooling at the neck is employed. By heat conduction of the tissue, the effect of cooling computed with the help of the discretization of heat gradient and heat conductivity of the local tissue propagates into the inner part of the domain. Concerning the blood flow, the averaging step within (3.4) captures the local cooling effect which results in a slightly cooler average temperature of the venous blood within the whole domain than in the initial state. Employing this value in (3.3) results in a slight negative change of the blood pool temperature. Taking account of the

evaluation of the source term (3.2) for the control volumes located in the vicinity of the neck, we notice that a strong cooling is locally equalized by the combination of a) the source term due to blood flow which is mostly influenced by the neutral blood temperature in the rest of the body and b) of the source term due to metabolic heat production which was not influenced at all by the change in the boundary temperature. The result is that the effect of a local cooling mechanism is instantly distributed over the whole domain while a weighted mean value of the temperature over the domain equalizes local cooling mechanisms. The validity of this reasoning is verified by numerical results [7, 2] and by an exemplary result shown in Section 6.

The non-local nature of the described blood flow model can directly be seen by applying an implicit time stepping strategy. Due to the integration over the whole computational domain in (3.4), one ends up with a fully occupied matrix after the usual linearization step which was already recognized in [7] in the context of steady state calculations.

We now illuminate a further property of the bloodflow model. Therefore, let the abbreviations $\alpha = \rho_B c_B$, $\beta = \int_D K_B(\mathbf{x})B(\mathbf{x})\,d\mathbf{x}$ and $\gamma = \rho_B/m_B$ hold. A straightforward computation gives

$$T_B(t) = T_V(t) - \frac{1}{\gamma\beta}\frac{d}{dt}T_B(t). \tag{3.5}$$

Note that α, β and γ are positive constants. Consider a steady state situation as initial state, i.e. $T_B = T_V$ holds. If the body is heated, the temperature within the body increases and so T_V will increase. This has the effect that the bloodpool temperature T_B will increase in the near future, i.e. $T_B'(t) > 0$. We now investigate the net effect of the bloodflow. Integration of the source over the computational domain D results in

$$\int_D Q_B(\mathbf{x},t)\,d\mathbf{x} = \alpha\left[\beta T_B(t) - \int_D K_B(\mathbf{x})B(\mathbf{x})T(\mathbf{x},t)\,d\mathbf{x}\right] \overset{(3.5)}{=} -\frac{\alpha}{\gamma}\frac{d}{dt}T_B(t).$$

When employing $T_B'(t) > 0$ we see that the total of all sources in the body is negative, i.e. while the blood in the bloodpool cools the increasingly warm body in the mean if the body is exposed to heat, it also takes over heat from it. The bloodpool and the body are to be seen as two separate systems which are connected via heat fluxes and so one can consider the bloodpool as a regulator.

4 Numerical method and experiments

The following numerical approximation of the unsteady bio-heat equation (3.1) represents a convenient extension of the finite volume method developed in [7], which has been proven to be a robust, accurate and reliable algorithm in the context of steady state temperature distributions. However, finite volume schemes are categorically based on the integral form of the governing equation. In order to apply Gauss's integral theorem it is neccessary to write the equation in divergence form. Therefore, we introduce the auxiliary variable $k(\mathbf{x}) = \rho(\mathbf{x})c(\mathbf{x})$ and the auxiliary temperature $\overline{T}(\mathbf{x},t) = k(\mathbf{x})T(\mathbf{x},t)$

into the governing equation and consequently the bio-heat equation (3.1) writes

$$\frac{d}{dt}\int_\sigma \overline{T}(\mathbf{x},t)\,d\mathbf{x} = \int_{\partial\sigma}\left[\frac{\lambda(\mathbf{x})}{k(\mathbf{x})}\nabla\overline{T}(\mathbf{x},t) - \frac{\lambda(\mathbf{x})\overline{T}(\mathbf{x},t)}{k(\mathbf{x})^2}\nabla k(\mathbf{x})\right]\cdot\mathbf{n}(\mathbf{x})\,\mathbf{ds} + \int_\sigma \mathbf{f}(\mathbf{x},\mathbf{t})\,\mathbf{dx} \tag{4.1}$$

for all control volumes $\sigma \subset D$, see [2]. In order to solve equation (4.1) numerically, the space part $\overline{D}$ is decomposed into a finite number of sub-domains. We start from an

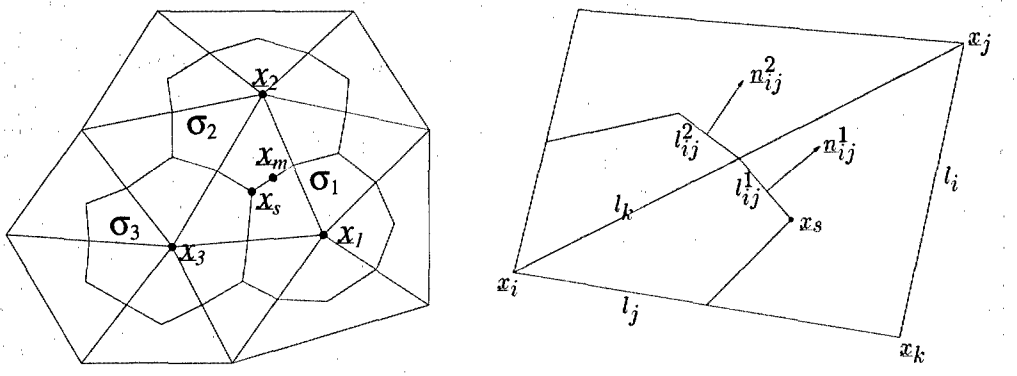

FIG. 1. General form of a control volume of the triangulation (left) and its boundary (right).

arbitrary conforming triangulation $\mathcal{D}^h$ of the domain $\overline{D}$ which is called the primary mesh and consisting of finitely many triangles $\mathcal{D}_i$ and the corresponding nodes are abbreviated by $\mathbf{x}_i \in \overline{D}$. Based on the triangulation a discrete control volume σ_i is defined as the open set of $\mathbf{R^2}$ including the node $\mathbf{x}_i$ and bounded by straight lines which are determined by the connection of the midpoints of the edges of the corresponding triangles $\mathcal{D}_j$ (i.e. $\mathbf{x}_i \in \partial\mathcal{D}_j$) and their barycentre (see Figure 1). The union $\mathcal{B}^h$ of all boxes is called the secondary mesh. A finite volume method represents a discretization of the evolutionary equation (4.1) for cell averages defined by $\left(\mathcal{M}\overline{T}\right)(t)\big|_\sigma = (1/|\sigma|)\int_\sigma \overline{T}(\mathbf{x},t)\,d\mathbf{x}$, where $|\sigma|$ denotes the volume of the box σ. With respect to the secondary mesh $\mathcal{B}^h$ we can write the integral form (4.1) as

$$\begin{aligned}\frac{d}{dt}\left(\mathcal{M}\overline{T}\right)(t)\big|_{\sigma_i} &= \frac{1}{|\sigma_i|}\left\{\int_{\partial\sigma_i}\left[\frac{\lambda(\mathbf{x})}{k(\mathbf{x})}\nabla\overline{T}(\mathbf{x},t) - \frac{\lambda(\mathbf{x})\overline{T}(\mathbf{x},t)}{k(\mathbf{x})^2}\nabla k(\mathbf{x})\right]\cdot\mathbf{n}(\mathbf{x})\,\mathbf{ds}\right.\\ &\left. + \int_{\sigma_i} Q_B(\mathbf{x},t)\,d\mathbf{x} + \int_{\sigma_i} Q_M(\mathbf{x})\,d\mathbf{x}\right\},\ \forall\sigma_i \in \mathcal{B}^h.\end{aligned} \tag{4.2}$$

Corresponding to a finite element method the evaluation of the boundary integral is performed by using a piecewise constant distribution of the heat coefficient λ and a piecewise linear distribution of the auxilary temperature $\overline{T}$. with respect to the triangles of the trianglutaion used. Note that the source term remains unchanged and the calculation is

given by

$$\int_{\sigma_i} Q_M(\mathbf{x})\, d\mathbf{x} = |\sigma_i| Q_M(\mathbf{x}_i)$$

and

$$\int_{\sigma_i} Q_B(\mathbf{x}, t)\, d\mathbf{x} = |\sigma_i| c_B \rho_B CCX(\mathbf{x}_i) BF(\mathbf{x}_i) \left[T_B(t) - T(\mathbf{x}_i, t)\right].$$

The computation of the blood pool temperature is directly performed by an explicit time discretization of equation (3.3). Thereby, the temperature of the venous blood is given by equation (3.4).

It is remarkable that the method degenerates to the scheme presented in [7] in the context of a steady state solution and therefore the excellent properties like the discrete min-max principle are maintained in such a situation. Due to the space available

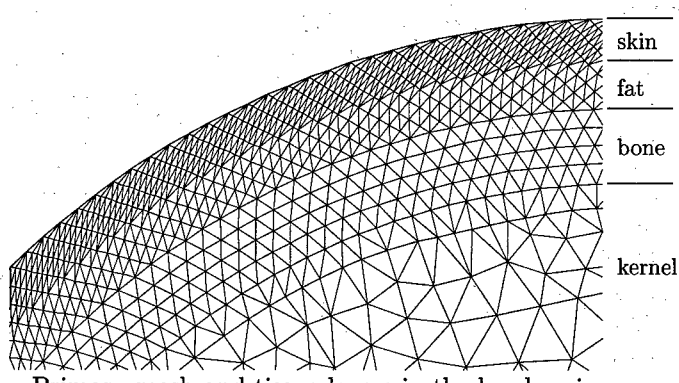

FIG. 2. Primary mesh and tissue layers in the head region.

we restrict ourself to the consideration of steady state calculations using the described method. Thereby, we distinguish layers of skin, fat, bone and kernel by different rates of metabolism, specific heat capacity and blood perfusion associated with the regions depicted in Figure 2. As boundary conditions we employ a comfortable boundary temperature of $309.15\,K$ at head, back, legs, and belly while we set $299.15\,K$ at the neck, i.e. we selectively cool the neck. In reality, this corresponds to the situation where the infant is wearing a water-filled collar with the purpose of cooling the blood flowing into the brain through the arteries adjacent to the skin.

In Figure 3 (a) we can see the temperature distribution in the two-dimensional discretized idealization of the body of a premature infant. Thereby, no blood flow and no metabolic heat production is applied, so that the depicted distribution of heat is only influenced by the heat conductivity of the employed tissues. The situation where tissue dependent metabolic heat production is taken into account is shown in Figure 3 (b). Note that the heat sources visualized within the picture not only have local effects, they also influence the mean value of the temperature of the blood pool. Within Figure 3 (c), blood flow is additionally given.

It is evident that the blood flow has the effect outlined in Section 5. Especially, the numerical solution incorporates no hint of the fact, that in reality there is a transport of cool blood to the brain and also a transport of blood by the veins coming from the brain.

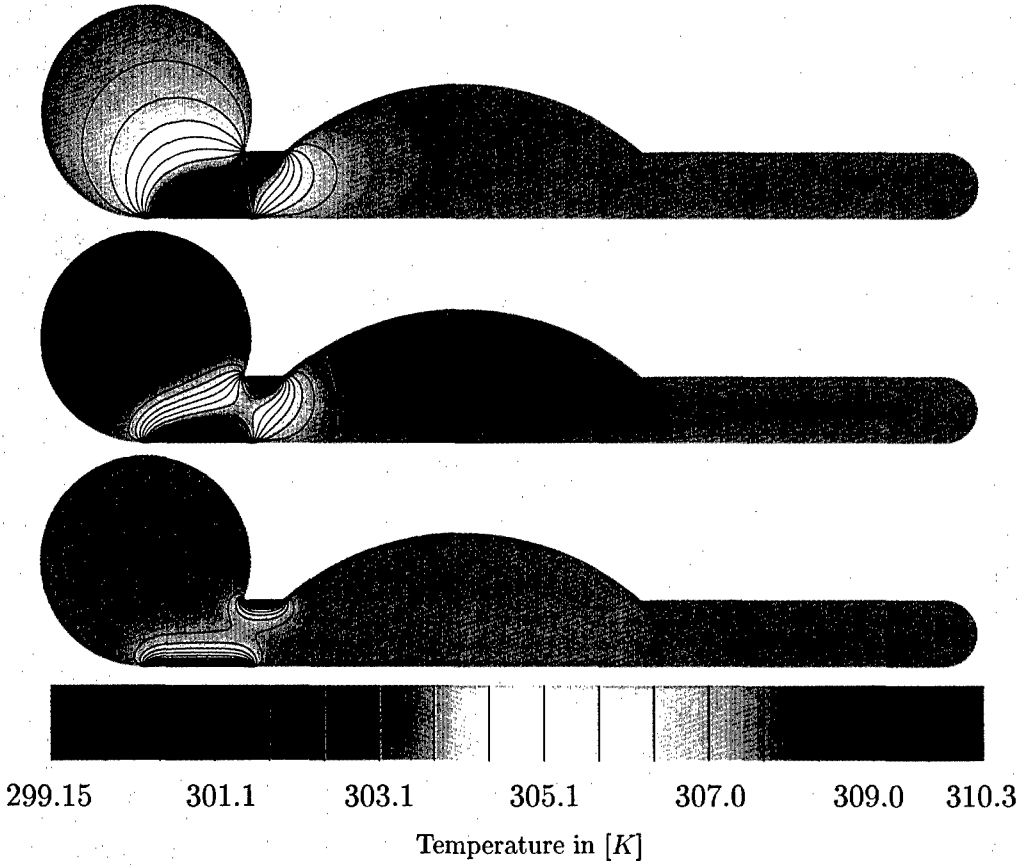

FIG. 3. Comparison of steady state situations (a) only with heat conduction (b) with heat conduction and metabolic heat production and (c) with blood flow additionally taken into account (from top to bottom).

5 Concluding remarks

The range of applicability of the described blood flow model is restricted to situations where it makes sense to employ a mean value of the whole blood, e.g. if the whole body is exposed for a longer time to the same temperature. For a clinical application where the effects of local cooling or heating have to be studied, caution is required when dealing with the results achieved by employing variations of the described model.

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